

In the specification

Please replace the paragraph on page 6, lines 4-5, with the following paragraph:

Figure 2 is a graph comparing the plasma levels of paclitaxel over time following oral administration of paclitaxel-poly(FA:SA) PIN formulations (A), (B), (C) with free paclitaxel.

Please replace the paragraph on page 6, lines 8-10, with the following paragraph:

Figure 4 is a bar graph comparing the relative bioavailability of paclitaxel (\pm SEM) for five different oral formulations.

Please replace the paragraph bridging pages 37 and 38, with the following paragraph:

Figure 3 ~~Figure 4~~ is a graph comparing the average relative bioavailability of different oral formulations. Six different paclitaxel-containing oral formulations were tested. The columns on Figure 3 ~~Figure 4~~ are described below from left to right. The height of each column represents the average relative bioavailability following oral administration of 48 mg paclitaxel/kg rat. Column A represents the results from the administration of 30% paclitaxel/PLGA -PIN formulation with bioadhesive excipients, which is described in Example 1 (160 mg formulation/kg rat). Column B represents results from the administration of a 30% paclitaxel/PLGA-PIN formulation without any bioadhesive excipients (160 mg formulation/kg rat). Column C represents results from the co-administration of a blank PLGA formulation containing bioadhesive excipients with free paclitaxel (160 mg formulation/kg rat). Column D represents results from the administration of free paclitaxel, agitated in 0.5% SLS/PBS to induce dissolution (48 mg formulation/kg rat). Column E represents results from the administration of paclitaxel micronized by PIN, which is described in Example 6 (48 mg formulation/kg rat). Column F represents results from the administration of a paclitaxel/PLGA-PIN formulation with

bioadhesive excipients (160 mg formulation/kg rat). All preparations were re-suspended for administration in 0.5% SLS/PBS, except for paclitaxel micronized by the phase-inversion (PIN) process (Formulation E) and Formulation F, which were re-suspended in distilled water (dH₂O). The excipients in Formulations A, C and F were Fumaric anhydride oligomers, Polyvinylpyrrolidone (PVP), and Iron Oxide (FeO, Fe₂O₃ and/or Fe₃O₄).

Please replace the paragraph on page 39, lines 17-24, with the following paragraph:

The relative bioavailability of paclitaxel/PLGA with excipients made using PIN was 8.5% (see Figure 3 ~~Figure 1~~, columns A and F). This result strongly contrasts the bioavailability of paclitaxel/PLGA without excipients which was 3.8% (column B) or paclitaxel alone at 2.4% (column E). Thus, the presence of PLGA and excipients clearly increases the relative bioavailability of the drug. Further, there appears to be no difference in relative bioavailability if the paclitaxel/PLGA was dispersed in 0.5% SLS/PBS (column A) or dH₂O (column F).

Please replace the paragraph on page 43, lines 16-26, with the following paragraph:

Since the low dose (< 10 mg/kg) intravenous (IV) pharmacokinetics of paclitaxel are not linear, the bioavailability of the orally administered drug is calculated relative to the IV dose that yields the same plasma area under the curve (AUC) value as observed for a given oral administration. To accomplish this, IV pharmacokinetic studies were performed at several doses, the resultant AUC's were determined, and an equation describing the dose/AUC relationship was fit to the data. This allows the calculation of the IV dose corresponding to the observed oral AUC. The fractional bioavailability (BA) of the oral dose is the ratio of the oral

formulation's corresponding IV dose to the actual oral dose (IV dose/Oral dose). The results of this bioavailability study are shown in Figure 4 ~~Figure 3~~.

Please replace the paragraph bridging pages 46 and 47, with the following paragraph:

The effect of the solvent:non-solvent ratio (during the PIN process) on the size of paclitaxel particles prepared by PIN was determined. The solvent was dichloromethane and the non-solvent was pentane. Samples were re-suspended and then measured immediately following a single 3-minute ~~3-minute~~ bath sonication. Particle sizing re-suspension medium was 1.0%(w/v) PVP/0.5%(w/v) SLS/PBS. Figure 5d shows the results for ratios of solvent dichloromethane:non-solvent pentane of 1:100 to 1:05. All ratios yielded nanoparticles. Dilution ratios of 1:100 (standard), 1:50, 1:25, 1:10 and 1:5 are illustrated. The 1:100 and 1:50 dilutions are essentially identical; the 1:25 dilution shows some increase in 0.3 - 0.5 micron range particles; and the particle size mode shifts to the 0.5 micron range at 1:10 and 1:5. The size distribution plot shows that this increase was not accompanied by significant expansion of particle size into the multi-micron size range. The effect of additional sonication was not explored. A dilution ratio of 1:1 was also tested. The drug precipitated as a macroscopic precipitate, with little evidence of fine particle creation; in one experiment, the precipitate spontaneously redissolved, implying that the 1:1 ratio is very close to the limiting concentration of pentane in dichloromethane in which paclitaxel is soluble. Temperature can also be a variable in solubility.